UKE Paper of the Month Februar 2021

The natural axis of transmitter receptor distribution in the human cerebral cortex

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ABSTRACT:
Transmitter receptors constitute a key component of the molecular machinery for intercellular communication in the brain. Recent efforts have mapped the density of diverse transmitter receptors across the human cerebral cortex with an unprecedented level of detail. Here, we distill these observations into key organizational principles. We demonstrate that receptor densities form a natural axis in the human cerebral cortex, reflecting decreases in differentiation at the level of laminar organization and a sensory-to-association axis at the functional level. Along this natural axis, key organizational principles are discerned: progressive molecular diversity (increase of the diversity of receptor density); excitation/inhibition (increase of the ratio of excitatory-to-inhibitory receptor density); and mirrored, orderly changes of the density of ionotropic and metabotropic receptors. The uncovered natural axis formed by the distribution of receptors aligns with the axis that is formed by other dimensions of cortical organization, such as the myelo- and cytoarchitectonic levels. Therefore, the uncovered natural axis constitutes a unifying organizational feature linking multiple dimensions of the cerebral cortex, thus bringing order to the heterogeneity of cortical organization.

STATEMENT:
Communication between cells in the brain relies on a plethora of different types of neurotransmitter receptors. What are organizational principles that make sense of the great diversity of such molecular signatures across the brain? In our study of the human cerebral cortex, which was conducted in the context of the Human Brain Project, we demonstrate that the distribution of receptors forms a natural axis that stretches from sensory to association areas. Traversing this axis entails changes in the diversity, excitability, and mirrored density of ionotropic and metabotropic receptors. These principles offer explanatory depth for diverse phenomena of brain structure, dynamics and function, and make concrete, testable predictions relevant in several fields of neuroscience. For instance, our study reveals that the excitatory nature of different parts of the brain is spatially ordered and can function as a template for predictions in a clinical context, e.g., predict the prevalence of epileptic foci, or the progression of neurodegenerative diseases. From a broader standpoint, our study showcases how the complexity of the brain can be harnessed, transitioning from empirical observations to fundamental principles.

BACKGROUND:
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